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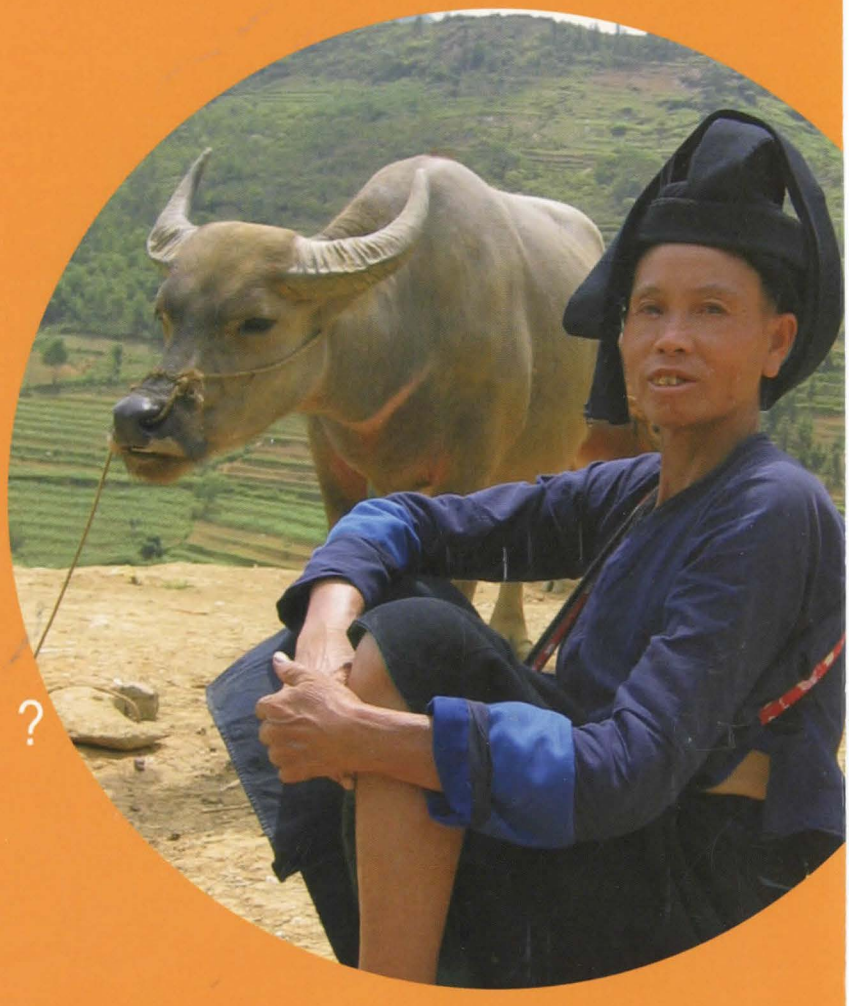

Does control of animal infectious risks offer a new international perspective ?

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AVIAN INFLUENZA VACCINE DEVELOPMENT, PRACTICAL APPLICATION IN DEVELOPING COUNTRIES

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ASBTRACT

Vaccination is a useful tool for the control of avian influenza (AI) outbreaks, but its use is forbidden in most countries worldwide because of its interference with AI screening tests and its negative impact on poultry trade. Currently licensed AI vaccines increase host resistance to the disease but have a limited impact on the virus transmission. To control or eradicate the disease, a carefully conceived vaccination strategy must be accompanied by strict bio-security measures. Some countries have, in the past, authorised vaccination under special circumstances with contrasting results, from control and disease eradication (USA, Italy) to endemism and antigenic drift of the viral strain (Mexico, Pakistan). Extensive vaccination programs are ongoing in Vietnam People's Republic of China and Indonesia to control the H5N1 epidemic. This paper provide practical information on the available AI vaccines and associated diagnostic tests, the vaccination strategies applied in Asia and their impact on the disease epidemiology.

INTRODUCTION

The control and eradication of highly pathogenic avian influenza (HPAI) have relied so far on stamping out of infected animals and biosecurity measures including quarantine, surveillance and hygiene. Strategies for the control of low pathogenic viruses (LPAI) have varied from no action to control with vaccination. However, AI vaccination is prohibited in most countries because of export bans on vaccinated animals. Recently the World Organisation for Animal Health (OIE) and the United Nation's Food and Agricultural Organisation (FAO) have recommended the use of vaccination against H5N1 HPAI virus in developing countries where mass culling of poultry is no longer acceptable for "ethical, ecological

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and economic reasons". However, AI vaccination has been empirical so far and rules that have been applied in Europe are obsolete in most of the developing countries where biosecurity standards and poultry raising systems are very different (Rushton, 2006). Mass vaccination against H5N1 HPAI is currently in use in China, Vietnam and Indonesia and to some extend in Egypt and Sudan. The aim of this presentation is to review practical issues on the AI vaccination campaigns which have been implemented to date in China and South East Asia.

AVIAN INFLUENZA VACCINES

An ideal veterinary vaccine should be safe, potent, thermostable, single dose, easy to administer and allows the differentiation between vaccinated and infected animals. Three different types of avian influenza vaccines against H5N1 virus are available on the market and in use in Asia: inactivated heterologous vaccines (H5N2; H5N9); recombinant inactivated homologous vaccines (reverse genetic (RG) H5N1) and live recombinant vaccines (H5 fowlpox and Newcastle viruses vectors (NDv)) (Capua and Marangon, 2006; Swayne, 2003). None of the avian influenza vaccines listed above satisfy the "ideal vaccine" criteria. All are cold chain dependant, a great limitation for developing countries where electric supply and cooling systems are not homogeneously available. They need to be parenterally injected via needles, a limiting factor in terms of labour and time in the case of mass vaccination of million of poultry. For inactivated vaccines multiple doses are necessary to confer protection. Only live vaccines could induce protection after a single dose but their efficacy might be impaired in adults because of previous natural infection. Differences have also been observed between laboratory and field efficacy for inactivated vaccines; especially in areas were immunosuppression with other circulating diseases (e.g. Gumboro disease) is happening.

UPDATE ON VACCINATION CAMPAIGNS

Hong Kong has been using European H5N2 and Chinese RGH5N1 inactivated vaccines for their mass vaccination program since 2002. Vaccination strategy and biosecurity measures have proven to be effective as no outbreak was reported from 2004 until now whereas a number of outbreaks occurred in adjacent regions of mainland China, Thailand, and Vietnam.

Mainland China produces and uses billions of doses of inactivated and live vaccines (H5N2, RGH5N1, fowlpox H5 and NDv H5) and exports to Vietnam and Indonesia. To date more than 5 billions of poultry have been vaccinated since 2004 which has probably helped limiting the occurrences of human cases.

Industrial farms in Vietnam or Indonesia have to pay for their own vaccination and import their vaccines from Europe or America. Vietnam government has been using Chinese H5N1 and H5N2 vaccines for their national campaigns since 2005. The disease has been controlled with the last human case in Dec 2005. New outbreaks in poultry have occurred since Dec 2006 but were rapidly contained. There is an incentive in Vietnam to set up a local vaccine production as it is already the case in Indonesia. One of the main issues in vaccine production is the capacity to assess the protective efficacy of the vaccines both in the laboratory and in the field prior to general use.

In Indonesia locally produced vaccines have been used for their national campaigns since 2005. Vaccine supply shortages along with specific practical issues for implementation of the campaigns have resulted in a limited coverage so far. The disease is still spreading along the islands and human cases are being accounted for each month.

VACCINATION STRATEGIES

AI vaccines increase host resistance to AI disease and reduce viral excretion therefore reducing the risk of contact infection within flocks (van der Goot *et al.,* 2005). However, protection is species dependant and varies also with the degree of homology between the vaccine strain and the circulating virus. Vaccination is only a tool and should be used along with the improvement of biosecurity measures. China, Vietnam and Indonesia are all applying mass vaccination programs with some specificity but they are all facing issues specific to developing countries:

– rational behind the choice of vaccine according to its homology with the circulating virus and efficacy in the targeted species (Webster *et al.,* 2006);

– post-vaccination surveillance to assess 1) the efficacy of vaccination and 2) monitor the antigenic drift of the field virus (Lee *et al.,* 2004). Lack of resources and organisational tools are limiting the application of efficient post-vaccination monitoring programs in most developing countries;

– information program on advantages and limitations of avian influenza vaccination: even in remote areas, farmers needs to be aware that

vaccination do not prevent infection and that multiple doses are required to confer immunity;
– choice of vaccination protocols: countries are facing practical and financial difficulties to implement mass vaccination (discrepancy between provincial strategies; low vaccination coverage; unavailability of vaccines). The sustainability of such vaccination strategy on a long term needs to be addressed (cost-benefit analysis);
– economic impacts: cost-effectiveness of different control strategies must be evaluated.

DISCUSSION

To effectively control the virus from circulating in poultry, an efficient post-vaccination surveillance program should be established. This appears to be the main challenge for developing countries along with the economical issues. A performing control and eradication programme should also include strict quarantines, movement controls on animals and equipment, strengthened biosecurity, extensive surveillance, and a comprehensive education programme for the public.

More research on vaccines optimisation is needed. To date, AI vaccines have not been used extensively and companies have not felt the need to focus research improving such vaccines. Even though numerous experimental AI vaccines are under development, basic data on efficacy of currently used vaccines are still lacking. Eradication of the disease within a poultry population will not be achieved if effective vaccines are not available for waterfowl.

New concerns recently have arisen regarding the illegal use of vaccines obtained from "underground" or "black" markets. The illegal use of AI vaccines has been reported in some countries where vaccination against AI is still prohibited. A thorough control and communication program on the benefits and limits of AI vaccination needs to be developed quickly and put in place.

AI vaccine markets are expanding. More developing countries are planning to produce their own vaccine to meet domestic need. However, it is difficult for a small country to compete with international pharmaceutical companies in the AI vaccine markets. Moreover they might be lacking the resources to set up "Quality control" and potency assessment of the vaccines.

CONCLUSION

Through the Asian experience, it has become clear that AI vaccination is already playing an essential part in the control of the actual H5N1 panzootic in developing countries. And its use will be quickly spreading to recently infected African countries. However, a case per case analysis should be performed in the decision making process to implement vaccination or not. New set of tools (risk modelling, economical models…) are required to help this decision making along with further research in the optimisation of avian influenza vaccines. There is also a great need to improve veterinary policy and capacity of veterinary services for a better control. Uncontrolled vaccination, including the improper distribution and administration of a vaccine and/or the use of bad vaccines, poses a greater threat in further outbreaks, which raises the possibility of potential mutation of the virus to become a pandemic pathogen.

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